General

Guideline Title

Metastatic pancreatic cancer: American Society of Clinical Oncology clinical practice guideline.

Bibliographic Source(s)

Sohal DP, Mangu PB, Khorana AA, Shah MA, Philip PA, O'Reilly EM, Uronis HE, Ramanathan RK, Crane CH, Engebretson A, Ruggiero JT, Copur MS, Lau M, Urba S, Laheru D. Metastatic pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2016 Aug 10;34(23):2784-96. [66 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

August 31, 2016 – Opioid pain and cough medicines combined with benzodiazepines : A U.S. Food and Drug Administration (FDA) review has found that the growing combined used of opioid medicines with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. FDA is adding Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines and benzodiazepines.

Recommendations

Major Recommendations

Definitions for the rating of evidence (High, Intermediate, Low, Insufficient); types of recommendations (Evidence based, Formal consensus, Informal consensus, No recommendation); and strength of recommendations (Strong, Moderate, Weak) are provided at the end of the "Major Recommendations"

field.

Clinical Question 1

After a histopathologic confirmation of pancreatic adenocarcinoma diagnosis, what initial assessment is recommended before initiating any therapy for metastatic pancreatic cancer?

Recommendation 1.1. A multiphase computed tomography (CT) scan of the chest, abdomen, and pelvis should be performed to assess extent of disease. Other staging studies should be performed only as dictated by symptoms (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 1.2. The baseline performance status (PS), symptom burden, and comorbidity profile of a patient with metastatic pancreatic cancer should be evaluated carefully (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 1.3. The goals of care (which include a discussion of an advance directive), patient preferences, and support systems should be discussed with every patient with metastatic pancreatic cancer and his or her caregivers (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 1.4. Multidisciplinary collaboration to formulate treatment and care plans and disease management for patients with metastatic pancreatic cancer should be the standard of care (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 1.5. Every patient with pancreatic cancer should be offered information about clinical trials, which include therapeutic trials in all lines of treatment as well as palliative care, biorepository/biomarker, and observational studies (Type: informal consensus, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Clinical Question 2

What is the appropriate first-line treatment of patients with metastatic pancreatic cancer?

Recommendation 2.1. Leucovorin, fluorouracil, irinotecan, and oxaliplatin (FOLFIRINOX) is recommended for patients who meet all of the following criteria: Eastern Cooperative Oncology Group (ECOG) PS 0 to 1, favorable comorbidity profile, patient preference and support system for aggressive medical therapy, and access to chemotherapy port and infusion pump management services (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 2.2. Gemcitabine plus nanoparticle albumin-bound (NAB)-paclitaxel is recommended for patients who meet all of the following criteria: ECOG PS 0 to 1, relatively favorable comorbidity profile, and patient preference and support system for relatively aggressive medical therapy (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 2.3. Gemcitabine alone is recommended for patients who have either an ECOG PS 2 or a comorbidity profile that precludes more-aggressive regimens and who wish to pursue cancer-directed therapy. The addition of either capecitabine or erlotinib to gemcitabine may be offered in this setting (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

Recommendation 2.4. Patients with an ECOG PS ≥3 or with poorly controlled comorbid conditions despite ongoing active medical care should be offered cancer-directed therapy on only a case-by-case basis. The major emphasis should be on optimizing supportive care measures (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

Clinical Question 3

What is the appropriate therapy for patients with metastatic pancreatic cancer who experience either

disease progression or intolerable toxicity with prior regimens for metastatic pancreatic cancer?

Recommendation 3.1. Gemcitabine plus NAB-paclitaxel can be offered as second-line therapy for patients who meet all of the following criteria: first-line treatment with FOLFIRINOX, ECOG PS 0 to 1, relatively favorable comorbidity profile, and patient preference and a support system for aggressive medical therapy (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: moderate).

Recommendation 3.2. Fluorouracil plus oxaliplatin, irinotecan, or nanoliposomal irinotecan can be offered as second-line therapy for patients who meet all of the following criteria: first-line treatment with gemcitabine plus NAB-paclitaxel, ECOG PS 0 to 1, relatively favorable comorbidity profile, patient preference and a support system for aggressive medical therapy, and chemotherapy port and infusion pump management (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: moderate).

Recommendation 3.3. Gemcitabine or fluorouracil can be considered as second-line therapy for patients who have either an ECOG PS of 2 or a comorbidity profile that precludes more-aggressive regimens and who wish to pursue cancer-directed therapy (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: moderate).

Recommendation 3.4. No data are available to recommend third-line (or greater) therapy with a cytotoxic agent. Clinical trial participation is encouraged (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: moderate).

Clinical Question 4

When should the concept of palliative care be introduced?

Recommendation 4.1. Patients with metastatic pancreatic cancer should have a full assessment of symptom burden, psychological status, and social supports as early as possible, preferably at the first visit. In most cases, this assessment will indicate a need for a formal palliative care consult and services (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Clinical Question 5

For patients with metastatic pancreatic cancer, what are the recommended strategies for relief of pain and symptoms?

Recommendation 5.1. Patients with metastatic pancreatic cancer should be offered aggressive treatment of the pain and symptoms of the cancer and/or the cancer-directed therapy (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Clinical Question 6

What is the recommended frequency of follow-up care/surveillance for patients with metastatic pancreatic cancer?

Recommendation 6.1. For patients on active cancer-directed therapy outside a clinical trial, imaging to assess first response should be offered at 2 to 3 months from the initiation of therapy. CT scans with contrast are the preferred modality. Thereafter, clinical assessment conducted frequently during visits for cancer-directed therapy should supplant imaging assessment. The routine use of positron emission tomography scans for the management of patients with pancreatic cancer is not recommended. Cancer antigen (CA) 19-9 is not considered an optimal substitute for imaging for assessing treatment response (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: strong).

Recommendation 6.2. No data exist on the duration of cancer-directed therapy. An ongoing discussion of goals of care and assessment of treatment response and tolerability should guide decisions to continue

or hold/terminate cancer-directed therapy (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: strong).

Definitions

Guide for Rating Quality of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits versus harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction of this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Guide for Types of Recommendations

Type of Recommendation	Definition
Evidence based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak"). The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement (see the "Availability of Companion Documents" field).
Informal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak").
No recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This

Rating for Strength of Recommendation	Definition
	is based on (1) good evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Metastatic pancreatic cancer

Guideline Category

Evaluation

Management

Treatment

Clinical Specialty

Gastroenterology

Oncology

Radiation Oncology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To provide evidence-based recommendations to oncologists and others for the treatment of patients with metastatic pancreatic cancer
- To help with clinical decision making, which includes the determination of the appropriate treatment of patients with metastatic pancreatic cancer and how to help patients and their families to access

and use palliative care services

Target Population

Patients with metastatic pancreatic cancer

Interventions and Practices Considered

Evaluation/Risk Assessment

- Multiphase computed tomography (CT) scan of the chest, abdomen, and pelvis
- Evaluation of baseline performance status, symptom burden, and comorbidity profile
- Discussion of goals of care (including a discussion of an advance directive), patient preferences, and support systems
- Early full assessment of symptom burden, psychological status, and social supports

Treatment/Management

- Multidisciplinary collaboration to formulate treatment and care plans and disease management
- Offering patients information about clinical trials, including therapeutic trials in all lines of treatment, as well as palliative care, biorepository/biomarker, and observational studies
- First-line therapy
  - FOLFIRINOX (leucovorin, fluorouracil, irinotecan, and oxaliplatin)
  - Gemcitabine plus nanoparticle albumin-bound (NAB)-paclitaxel
  - Gemcitabine alone (with or without capecitabine or erlotinib)
  - Offering therapy on a case-by-case basis in patients with poor performance status
- Second-line therapy
  - Gemcitabine plus NAB-paclitaxel
  - Fluorouracil plus oxaliplatin, irinotecan, or nanoliposomal irinotecan
  - Gemcitabine or fluorouracil
- Referring patients to clinical trials
- Aggressive treatment for pain and other symptoms
- Frequency of follow-up imaging (CT scans) (positron emission tomography [PET]/CT] not recommended)

Major Outcomes Considered

- Response rates
- Overall survival
- Disease-free survival
- Progression-free survival
- Adverse events

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The recommendations were developed by the multidisciplinary Expert Panel using a systematic review of articles in English (April 2002 to June 2015) of phase III randomized controlled trials (RCTs) of chemotherapy alone and/or chemoradiotherapy and/or compared with a control arm. Other peer-reviewed articles were used to inform the recommendations on palliative care, patients with metastatic pancreatic cancer, and clinician communication as well as the section on health disparities. Articles were excluded from the systematic review if they were meeting abstracts not subsequently published in peer-reviewed journals; editorials, commentaries, letters, news articles, case reports, or narrative reviews; and published in a non-English language.

Literature Search Strategy

Computerized literature searches of MEDLINE and the Cochrane Collaboration Library were performed. The searches of the English-language literature published from January 2000 to June 2015 combined pancreatic neoplasm terms and follow-up-related terms and MeSH headings. Results of the databases searches were supplemented with hand searching of the bibliographies of systematic reviews and selected seminal articles, and contributions from Expert Panel members' personal files.

Details of the literature search strategy are provided in Data Supplement 3 (see the "Availability of Companion Documents" field). A Quality of Reporting of Meta-analyses (QUOROM) Diagram that describes the article selection process is available in Data Supplement 4 (see the "Availability of Companion Documents" field).

Number of Source Documents

Twenty-five randomized controlled trials (RCTs) met the eligibility criteria and form the evidentiary basis for the guideline recommendations. Nine systematic reviews or meta-analyses of various rigor and quality were obtained; none were deemed suitable as the basis for recommendations.

See the Quality of Reporting of Meta-analyses (QUOROM) Diagram (Data Supplement 4) in the Data Supplement (see the "Availability of Companion Documents" field) for an outline of the study selection process.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Guide for Rating Quality of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits versus harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
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Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction of this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect.

Rating for Strength of Evidence	Definition
	Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Guide for Rating of Potential for Bias

Rating of Potential for Bias	Definitions for Rating Potential for Risk of Bias in Randomized Controlled Trials
Low risk	No major features in the study that risk biased results, and none of the limitations are thought to decrease the validity of the conclusions. The study avoids problems such as failure to apply true randomization, selection of a population unrepresentative of the target patients, high dropout rates, and no intention-to-treat analysis; and key study features are described clearly (including the population, setting, interventions, comparison groups, measurement of outcomes, and reasons for dropouts).
Intermediate	The study is susceptible to some bias, but flaws are not sufficient to invalidate the results. Enough of the items introduce some uncertainty about the validity of the conclusions. The study does not meet all the criteria required for a rating of good quality, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.
High risk	There are significant flaws that imply biases of various types that may invalidate the results. Several of the items introduce serious uncertainty about the validity of the conclusions. The study has serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Extraction

Literature search results were reviewed and deemed appropriate for full text review by two American Society of Clinical Oncology (ASCO) staff reviewers in consultation with the Expert Panel Co-Chairs. Data were extracted by two staff reviewers and subsequently checked for accuracy through an audit of the data by another ASCO staff member. Disagreements were resolved through discussion and consultation with the Co-Chairs if necessary. Evidence tables are provided in Data Supplements 1 and 2 (see the "Availability of Companion Documents" field).

Study Quality Assessment

Study design aspects related to individual study quality, strength of evidence, strength of recommendations, and risk of bias were assessed and are shown in Data Supplement 1, Table 2 (see the "Availability of Companion Documents" field). The study quality was high for this group of randomized controlled trials (RCTs). Design aspects related to the individual study quality were assessed with respect to factors such as blinding, allocation concealment, placebo control, intention to treat, funding sources, and so on, which generally indicated a low potential risk of bias for most of the identified evidence. Follow-up times varied among studies, which decreases the comparability of the results. Refer to the "Rating Scheme for the Strength of the Evidence" field for definitions of ratings for overall potential risk of bias.

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Panel Composition

The American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines Committee (CPGC) convened an Expert Panel with multidisciplinary representation in medical oncology, radiation oncology, surgical oncology, pathology, community oncology, patient/advocacy representation, and guideline implementation. The Expert Panel was led by two Co-Chairs who had primary responsibility for the development and timely completion of the guideline.

Guideline Development Process

The Expert Panel met via webinar on several occasions and corresponded frequently through e-mail; progress on guideline development was driven primarily by the Co-Chairs along with ASCO staff. The purpose of the meetings was for members to contribute content, provide critical review, interpret evidence, and finalize the guideline recommendations based upon the consideration of the evidence. All members of the Expert Panel participated in the preparation of the draft guideline document.

Development of Recommendations

The guideline recommendations were crafted, in part, using the GuideLines Into DEcision Support (GLIDES) methodology and accompanying BRIDGE-Wiz software™. This method helps guideline panels systematically develop clear, translatable, and implementable recommendations using natural language, based on the evidence and assessment of its quality to increase usability for end users. The process incorporates distilling the actions involved, identifying who will carry them out, to whom, under what circumstances, and clarifying if and how end users can carry out the actions consistently. This process helps the Panel focus the discussion, avoid using unnecessary and/or ambiguous language, and clearly state its intentions.

Rating Scheme for the Strength of the Recommendations

Guide for Types of Recommendations

Type of Recommendation	Definition
Evidence based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
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No recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Cost Analysis

Cost Implications

Limited cost-effectiveness analyses exist with regard to the various treatment modalities used in the multidisciplinary management of metastatic pancreatic cancer. However, the available data appear to support the recommendations in this guideline. One study assessed the cost-effectiveness of first-line FOLFIRINOX (leucovorin, fluorouracil, irinotecan, and oxaliplatin) compared with first-line gemcitabine for public payers in Canada. Compared with first-line gemcitabine, first-line FOLFIRINOX resulted in more life-years and quality-adjusted life-years. Probabilistic sensitivity analysis results showed that for analyses 1 and 2, respectively, FOLFIRINOX has a >85% probability and an approximately 80% probability of being cost-effective at the $100,000 threshold. Compared with gemcitabine, first-line FOLFIRINOX significantly prolongs median overall survival (OS). Given the favorable cost per quality-adjusted life-year, the improvement in clinical efficacy, and the limited available treatment options, FOLFIRINOX represents an attractive cost-effective treatment.

As reported at the 2014 Gastrointestinal Cancers Symposium, investigators compared the costs and clinical outcomes of gemcitabine plus nanoparticle albumin-bound (NAB)-paclitaxel versus erlotinib plus gemcitabine (E/G) by using drug cost per cycle multiplied by the median cycles delivered from clinical trials for gemcitabine plus NAB-paclitaxel and E/G. The comparison included the cost of the drugs as well as expenses related to the administration of the therapy and the management of adverse effects (AEs) of grade 3/4 severity. These costs were based on 4 months of therapy for gemcitabine plus NAB-paclitaxel versus 3.9 months for E/G as administered at a large, multisite oncology clinic. The researchers found that the total cost for gemcitabine plus NAB paclitaxel was $24,984 versus $23,044 for E/G. However, the gemcitabine plus NAB-paclitaxel is expected to deliver a greater survival benefit based on clinical trial data, bringing the cost per life-year gained to $15,522.

Moreover, health care experts have noted that the costs of treatment are high and increasing. The choice of therapy depends on a variety of clinical factors. More than 70% of cases are diagnosed in patients age 65 years and older. Thus, in the United States, Medicare pays for a substantial portion of associated costs. The costs of treating the malignancy are noteworthy when one considers that pancreatic cancer is the fourth leading cause of cancer-related mortality in the United States.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Members of the Expert Panel were responsible for reviewing and approving the penultimate version of guideline, which was then circulated for external review and submitted to *Journal of Clinical Oncology* for editorial review and consideration for publication. All American Society of Clinical Oncology (ASCO) guidelines are ultimately reviewed and approved by the Expert Panel and the ASCO Clinical Practice Guidelines Committee before publication. The Clinical Practice Guidelines Committee approved the guideline on October 21, 2015.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Current multiagent chemotherapy regimens afford some gains in overall survival, albeit with attendant treatment-emergent toxicities. The clinical course of pancreatic cancer usually is aggressive, with high symptom burden and potential for a substantial deterioration in quality of life. Palliative care to focus on distressing symptoms and quality of life is an important adjunct in the management of this condition.
- All patients can benefit from a discussion of their psychosocial concerns and their available support system.

Refer to the "Literature review and analysis" and "Clinical interpretation" sections of the original guideline document for a discussion of the potential benefits and harms of each recommendation.

Potential Harms

- Adverse effects and decreased effectiveness may limit the use of medications.
- In the FOLFIRINOX (leucovorin, fluorouracil, irinotecan, and oxaliplatin) trials, major grade 3 or 4 toxicities with FOLFIRINOX were neutropenia (46%), febrile neutropenia (5%), fatigue (24%), vomiting (15%), diarrhea (13%), and peripheral neuropathy (9%).
- In the gemcitabine plus nanoparticle albumin-bound (NAB)-paclitaxel trial, major grade 3 or 4 toxicities with gemcitabine plus NAB-paclitaxel were neutropenia (38%), febrile neutropenia (3%), fatigue (17%), diarrhea (6%), and peripheral neuropathy (17%).

Refer to the "Literature review and analysis" and "Clinical interpretation" sections of the original guideline document for a discussion of the potential benefits and harms of each recommendation.

Qualifying Statements

Qualifying Statements

- The clinical practice guidelines and other guidance published herein are provided by the American Society of Clinical Oncology, Inc. (ASCO) to assist providers in clinical decision making. The information herein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular course of medical care. Further, the information is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. Recommendations reflect high, moderate, or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicates that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in individual cases. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. ASCO provides this information on an "as is" basis and makes no warranty, express or implied, regarding the information. ASCO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ASCO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information, or for any errors or omissions.
- Refer to the "Health Disparities," "MCCs" and "Limitation of the Research and Future Directions" sections in the original guideline document for additional qualifying information.

Implementation of the Guideline

Description of Implementation Strategy

Guideline Implementation

American Society of Clinical Oncology (ASCO) guidelines are developed for implementation across health settings. Barriers to implementation include the need to increase awareness of the guideline recommendations among frontline practitioners, cancer survivors, and caregivers and to provide adequate services in the face of limited resources. The guideline Bottom Line Box was designed to facilitate implementation of recommendations. This guideline will be distributed widely through the ASCO Practice Guideline Implementation Network. ASCO guidelines are posted on the ASCO Web site and most often published in *Journal of Clinical Oncology* (*JCO*) and *Journal of Oncology Practice*.

For additional information on the ASCO implementation strategy, please see the ASCO Web site.

Implementation Tools

Patient Resources

Quick Reference Guides/Physician Guides

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Sohal DP, Mangu PB, Khorana AA, Shah MA, Philip PA, O'Reilly EM, Uronis HE, Ramanathan RK, Crane CH, Engebretson A, Ruggiero JT, Copur MS, Lau M, Urba S, Laheru D. Metastatic pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2016 Aug 10;34(23):2784-96. [66 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Aug 10

Guideline Developer(s)

American Society of Clinical Oncology - Medical Specialty Society

Source(s) of Funding

American Society of Clinical Oncology (ASCO)

Guideline Committee

Composition of Group That Authored the Guideline

Expert Panel Members: Davendra P.S. Sohal, MD, MPH (*Co-chair*), Cleveland Clinic, Cleveland, OH; Daniel Laheru, MD (*Co-chair*), Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; Alok A. Khorana, MD, Cleveland Clinic, Cleveland, OH; Manish A. Shah, MD, The Weill Cornell Medical Center, New York, NY; Eileen M. O'Reilly, MD, Memorial Sloan Kettering Cancer Center, New York, NY; Hope E. Uronis, MD, Duke University, Durham, NC; Ramesh K. Ramanathan, MD, Mayo Clinic, Scottsdale, AZ; Christopher H. Crane, MD, The University of Texas MD Anderson Cancer Center, Houston, TX; Philip A. Philip, MD, PhD, Karmanos Cancer Institute, Detroit, MI; Anitra Engebretson, patient representative, Portland, OR; Joseph T. Ruggiero, MD, Weill Cornell Medical College, New York, NY; Mehmet S. Copur, MD (*Practice Guideline Implementation Network [PGIN] representative*), St. Francis Medical Center, Grand Island, NE; Michelle Lau (*PGIN representative*), private practice, Tempe, AZ; Susan Urba, MD, University of Michigan Cancer Center, Ann Arbor, MI; Pamela B. Mangu, MA, American Society of Clinical Oncology (ASCO) staff

Financial Disclosures/Conflicts of Interest

Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with the American Society of Clinical Oncology's (ASCO's) Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at http://www.asco.org/rwc). All members of the panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting or advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the panel did not disclose any relationships constituting a conflict under the Policy.

Authors' Disclosures and Potential Conflicts of Interest

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Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Journal of Clinical Oncology Web site .

Availability of Companion Documents

The following are available:

Metastatic pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. Methodology supplement. Alexandria (VA): American Society of Clinical Oncology; 2016. 18 p. Available from the American Society of Clinical Oncology (ASCO) Web site .

Metastatic pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. Data supplement. Alexandria (VA): American Society of Clinical Oncology; 2016. 41 p. Available from the ASCO Web site .

Metastatic pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. Slide set. Alexandria (VA): American Society of Clinical Oncology; 2016. 22 p. Available from the ASCO Web site .

Metastatic pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. Summary of recommendations. Alexandria (VA): American Society of Clinical Oncology; 2016. 4 p. Available from the ASCO Web site .

Patient Resources

The following is available:

Pancreatic cancer - treatment options. Patient information. 2016 May 31. Available from the Cancer.Net Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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